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Gabapentin for Perioperative Pain Relief in Surgical Abortion

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STUDY PROTOCOL AND STATISTICAL ANAYLSIS PLAN

Procedures and Patient Enrollment

This study was approved by the University of Nevada, Reno Institutional Review Board (#734274). We used a double-blind placebo controlled trial of gabapentin in the setting of an ambulatory surgical abortion center where patients received routine intravenous sedation (IVS) consisting of midazolam 4mg, fentanyl 100mcg, and local para-cervical 1% lidocaine block anesthesia (PCB) plus either 600 mg of gabapentin or placebo 1-2 hours prior to surgery. Patients scheduled to undergo surgical abortion between 5 and 23 6/7 weeks by Ultrasound gestational age (UGA) were approached during the preoperative counseling and offered participation. Patients included were 18 years of age or older, speaking English or Spanish, and eligible for office based surgical pregnancy termination. Exclusion criteria included severe renal disease, current use of gabapentin or pregabin, sensitivity or allergy to gabapentin, a contraindication to gabapentin, or missed abortion. Participants were not compensated and could withdraw from the study at any time.

The allocation and concealment method used was sequentially numbered, opaque pill containers, containing either gabapentin or placebo in identical appearing capsules. Randomization of these sequential containers was done by balanced fixed blocks of six using a random number generator to determine placebo from treatment. Both the patients and providers were blinded to the study interventions.

Recruitment was sequential and based on the patient qualifying and consenting to the study. A standardized script was used. All study staff were trained in the procedures and provided with a study protocol prior to beginning of the study. A standard operations manual was available to the study staff to refer to for operational details. The study investigators provided instructions concerning the recording of study data on clinical research forms. The study investigators had the responsibility to assure the quality of computerized data, the protocol development and the final study databases.

Screening was done using a standardized checklist and the informed consent was reviewed with all eligible participants. Once consent was obtained and signed, the participants received the randomized pre-medication. Treatment bottles had been sequentially numbered so that par ticipants received the next available bottle in the sequence as they were recruited. Participants took the medication in front of the research staff. Baseline information was collected including age, marital and household status, race/ethnic group, gravidity, parity, LMP, gestational age, BMI, past medical and surgical history, medications, recreational drug use, prior abortions, and menstrual pain.

A master list for the randomized treatments was generated by the pharmacy staff and maintained by University staff. Unblinding was only available to the investigators after participants had completed treatment (more than 24 hrs).

Patients received Misoprostol 400 mcg buccal 90 minutes prior to surgery who were more than 12 weeks by ultrasound (UGA). Those patients more than 17 weeks by UGA had laminaria placed 1 day prior to surgery and patients at 20 to 23 6/7 weeks by UGA had laminaria placed over 2 days as well as digoxin 1mg intrafetal injection 2 days prior to surgery. All procedures were performed by the attending physician and residents who were trained and credentialed for these procedures.

Patient questionnaires using 100mm visual analog scales (VAS) were used by study staff prior to surgery and at 5 and 30 minutes after the procedure was completed as defined by speculum removal. We determined that our primary outcome measure was the pain score at 5 minutes as measured by the VAS scale. Secondary measures included pain at 30 minutes and 24 hrs following surgery, nausea and vomiting pre and postoperatively, pre-procedure pain, and anxiety using the VAS scales. Postoperatively patients received oxycodone 7.5 mg (quantity 10) for pain control at home. The 24 hours follow up contact was completed telephonically and included a study questionnaire.

Power calculations were performed to detect a 20-25-point VAS score difference between the treatment and placebo groups as we determined that this would be clinically relevant based on other

pain studies. This calculation yielded a need for approximately 100 patients in each arm based on 80% power and a type one error of 0.05.

Statistical Procedures and Data Analysis

All data were transcribed from the clinical research forms into REDCap (institutionally managed by University of Nevada, Reno), a web-based, password protected relational database and forms were secured in locked files. Data were subsequently imported into SPSS (v. 25) for analyses. Potential differences in socio-demographic variables were examined using chi-square analyses with Bonferroni-corrected post-hoc comparisons, except for "age", which was tested using an independent-samples t-test. Examination of VAS scores demonstrated skewness issues, and hence data were rank transformed for these variables. Mann-Whitney tests were utilized for comparing the treatment arms on outcomes with VAS measurements, except for pain. The pain variable was time-based, and hence we examined potential temporal trends in pain at 5 minutes, 30 minutes, and 24 hours post-procedure using a repeated-measures general linear model with baseline pain as a covariate; the RM-ANOVA provided the same statistical interpretation as the rank-based transformation, and hence the standard RM-ANOVA results are presented below.